UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND TOXIC SUBSTANCES

08/DEC/2000

MEMORANDUM

Subject: EPA Reg. No: 66222-GL Rimon 10EC
DP Barcodes: D263782
Case No: 065088
PC Code: 124002

From: Masih Hashim, Toxicologist
Technical Review Branch
Registration Division (7505C)

To: Suku Oonnithan, PM Team 04
Insecticide-Rodenticide Branch
Registration Division (7505C)

Applicant: Makhteshim-Agan of North America
551 Fifth Avenue
New York, NY 10176

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Novaluron	10.0
Inert Ingredients	90.0
Total:	100.0

Note: This Memo supercedes the previous one from 8-8-00.

Acute Tox

BACKGROUND: Makhteshim-Agan of North America has submitted a set of acute toxicity studies (MRID 449645-01 through 06) to support the registration of its Product Rimon 10EC, File Symbol 66222-GL. These studies were conducted at the Huntingdon Life Sciences, England and Medcon Laboratories, Sudkampen, Walsrode.

RECOMMENDATIONS: Five studies; acute oral, acute dermal, eye irritation, dermal irritation and guinea pig sensitization are in accordance with the Sub-Division F guidelines.

The Company submitted a waiver request for the inhalation study. If HED determines that the technical product has $LC_{50} > 5.15$ mg/L, the product will have low inhalation toxicity (Table 2 of letter 9-9-99). The Company also assured that the product will not pose inhalation hazard. Therefore, TRB grants a waiver for this study.

One correction is required in the percentages and decimal place for the column 13 of CSF dated November 4, 1999, so that it properly reflects the label and the Bean Sheet.

The toxicology profile for the File Symbol 66222-GL is as follows:

acute oral toxicity	IV	acceptable
acute dermal toxicity	III	acceptable
acute inhalation toxicity	IV	waived
primary eye irritation	II	acceptable
primary skin irritation	III	acceptable
dermal sensitization	pos.	acceptable-1998
dermal sensitization	neg.	unacceptable (data gap)

LABELING:

ID #: 066222-00035 Rimon 10EC

RESTRICTED USE CLASSIFICATION RECOMMENDED:

Due to eye irritation toxicity category.

The PM Team should decide if restricted use classification is necessary or if alternative labeling will allay the requirement for restricted use classification.

SIGNAL WORD: WARNING

PRECAUTIONARY STATEMENTS:

Causes substantial but temporary eye injury. Harmful if absorbed through skin. Do not get in eyes or on clothing. Avoid contact with skin. Wear goggles or face shield. Remove contaminated clothing and wash clothing before reuse. Prolonged or frequently repeated skin contact may cause allergic reaction in some individuals

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF SWALLOWED: Call a poison control center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to by a poison control center or doctor. Do not give anything by mouth to an unconscious person.

IF ON SKIN OR CLOTHING: Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.

IF IN EYES: Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call poison control center or doctor for treatment advice.

NOTE TO PHYSICIAN:

Note to PM/CRM/Registrant: The proposed label should contain a "Note to Physician." The following statements are suggested types of information that may be included, if applicable:

- technical information on symptomatology;
- use of supportive treatments to maintain life functions;
- medicine that will counteract the specific physiological effects of the pesticide;
- company telephone number to specific medical personnel who can provide specialized medical advice.

The following "Note to Physician" statement is required for the subject product:

Probable mucosal damage may contraindicate the use of gastric lavage.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (870.1100)

Product Manager: 04
MRID No.: 449645-01

EPA Reviewer: M Hashim
Study Completion Date: 9-30-96
Study No.: MBS 70

Testing Facility: Huntingdon Life Sciences, Cambridge, England
Author: L.A. McRae
Quality Assurance (40 CFR §160.12): Included

Test Material: Rimon 10EC
Species: Rats/CD
Age: 8-12 weeks
Weight: 200-229
Source: Harlan UK, Bicester, Oxon, England

Conclusion:

1. LD_{50} (mg/kg):
   Males: >5000 mg/kg
   Females: >5000 mg/kg
   Combined: >5000 mg/kg
2. The estimated LD_{50} is >5000 mg/kg
3. Tox. Category: IV Classification: Acceptable

Procedure (Deviations): None

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

Observations: Most rats showed pilo-erection, hunched posture, lethargy, wadling gait, decrease in respiratory rate, and bright yellow stained urine. A few rats showed pallor of the extremities, liquid feces, increased salivation and unsteadiness.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (870.1200)

Product Manager: 04
MRID No.: 449645-02

EPA Reviewer: M Hashim
Study Completion Date: 9-30-96
Study No.: MBS 67

Testing Facility: Huntingdon Life Sciences, Cambridge, England
Author: L.A. McRae
Quality Assurance (40 CFR §160.12): Included

Test Material: Rimon 10EC
Species: Rats/CD
Age: 8-12 weeks
Weight: 233-290
Source: Harlan UK, Bicester, Oxon, England

Conclusion:

1. Dermal LD_{50} (mg/kg):
   Males: >2000 mg/kg
   Females: >2000 mg/kg
   Combined: > 2000 mg/kg
2. The estimated LD_{50} is > 2000 mg/kg
3. Tox. Category: III Classification: Acceptable

Procedure (Deviations): None

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
2000	0/5	0/5	0/10

Observations: Slight Erythema and edema were noted in one animal through 4-10 days. Desquamation of the skin was seen in 2 animals.

Gross Necropsy: Unremarkable.

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (870.2400)

Product Manager: 04
MRID No.: 449645-03

EPA Reviewer: M Hashim
Study Completion Date: 9-2-96
Study No.: 10-03-0202/00-96

Testing Facility: Medcon Lab
Author: D. Honack
Quality Assurance (40 CFR §160.12): Included

Test Material: Rimon 10EC
Dose: 0.1 ml in the eye
Species: Rabbit/NZW
Source: E A Prinzhorn, Alterbucker Damm 38

Quality Assurance (40 CFR §160.12): Included

Conclusion:

1. Toxicity Category: II
2. Classification: Acceptable

Procedure (Deviations): Age and weight of the rabbit is not recorded.

Lesion	I h	24 h	48 h	72 h	4 d	5 d	6 d	7 d	8 d	9 d
corneal opacity	2/3	3/3	3/3	3/3	3/3	3/3	3/3	3/3	3/3	3/3
Iritis	0/3	1/3	3/3	3/3	3/3	3/3	2/3	2/3	2/3	2/3
conjunctivitis	2/3	3/3	3/3	3/3	0/3	0/3	0/3	0/3	0/3	0/3

Comments: Two is a positive score for conjunctiva and 1 for cornea and iris.
Corneal lesion remained in one animal up to 15 days. The test substance is a severe irritant.

DATA REVIEW FOR PRIMARY DERMAL IRRITATION TESTING (870.2500)

Product Manager: 04
MRID No.: 449645-04

EPA Reviewer: M Hashim
Study Completion Date: 9-19-96
Study No.: MBS 68

Testing Facility: Huntingdon Life Sciences, UK
Author: Brenda Parcell
Quality Assurance (40 CFR §160.12): Included

Test Material: Rimon 10EC
Dose: 0.5 ml
Species: Rabbit/NZW
Source: Charles River, UK
Age: 11-14 weeks
Weight: 2.3-3.2 kg

Conclusion:

1. Toxicity Category: III
2. Classification: Acceptable

Procedure (Deviations): The exact scores for PDIS are not given.

Rabbits showed erythema, edema, and desquamation of the stratum corneum. These lesions subsided by day 11. TRB has classified the product as moderately irritant.

DATA REVIEW FOR TESTING OF DERMAL SENSITIZATION (870.2600)

Product Manager: 04
MRID No.: 449645- 05

EPA Reviewer: M Hashim
Study Completion Date: 2-13-98
Study No.: , MAK/467

Testing Facility: Huntingdon Life Sciences, UK
Author: David Coleman
Quality Assurance (40 CFR §160.12): Included

Test Material: Rimon 10EC
Positive Control: HCA

Species: Guinea pigs/Hartley
Source: D. Hall, UK
Age: 4-7 weeks
Weight: 268-424 g

Conclusion: 1- The test substance is a dermal sensitizer 2- Acceptable

Procedure (Deviations): None

Method: Magnussaon and Kligman/Maximization

Based on a preliminary study intradermal injection was 0.5% v/v in water
Topical application as applied.
Challenge application 30% and 15% v/v in distilled water.
Dose levels for HCA were determined by the periodic historical control.
The test results showed that 12 of 20 animals showed positive response to dermal reaction/sensitization.

Based on this study the product is a dermal sensitizer.

DATA REVIEW FOR TESTING OF DERMAL SENSITIZATION (870.2600)

Product Manager: 04
MRID No.: 449645- 06

EPA Reviewer: M Hashim
Study Completion Date: 4-21-99
Study No.: , MAK/516

Testing Facility: Huntingdon Life Sciences, UK
Author: David Coleman
Quality Assurance (40 CFR §160.12): Included

Test Material: Rimon 10EC
Positive Control: HCA

Species: Guinea pigs/Hartley
Source: D. Hall, UK
Age: 4-7 weeks
Weight: 362-438 g

Conclusion: 1- non sensitizing 2- Unacceptable

Procedure (Deviations): None

Method: Buehler Method

The test group had 20 animals, with 10 animals as negative control, and the Positive Control had 20 animals (historical control). The animals were first induced for 3 weeks (9 exposures), and then challenged in accordance with the Buehler method.

The concentration of the test substance was full strength for induction, and 0.1% v/v in dist. water for challenge.

For positive control, there was full strength for induction and challenge was 50% v/v in Alembicol D for challenge.

Results: There was some reaction in the last phase of induction for the test animals. Finally at challenge with 0.1 % concentration gave negative reaction.

Comments:

An earlier test in 1998 MRID 44945-05 (see last page) showed positive results to sensitization. This test is supposed to be more sensitive for this kind of study. The current test with the same compound produced negative data using Buehler method. The selection for the concentration of the challenge dose is confusing, because the highest non reactive concentration tested in screening was 100% page 31 (449645-06). The rationale for using 0.10% as a challenge dose is questionable.

TRB concludes that the product has the potential for sensitization reaction.

ACUTE TOX ONE-LINERS

1. DP BARCODE: D263782
2. PC CODE: 124002
3. CURRENT DATE: 8-7-00
4. TEST MATERIAL: Novaluron 10%

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat/ Huntingdon / MBS 70/ 9-30-96	449645-01	LD_{50} >5000 mg/kg	IV	A
Acute dermal toxicity/ rat/Huntingdon/ MBS 67/962160/AC/ 9-30-96	449645-02	LD_{50} >2000 mg/kg	III	A
Acute inhalation toxicity	-	-	IV	W
Primary eye irritation /rabbit/ Medcon/ 10-03-0202/00-96/ 9-2-96	449645-03	severe irritant	II	A
Primary dermal irritation/rabbit/ Huntingdon / MBS68/ 9-19-96	449645-04	moderately irritant	III	A
Dermal sensitization guinea pig/ Huntingdon /MAK467 2-13-98	449645-05	sensitizer	-	A
Dermal sensitization guinea pig/ Huntingdon /MAK516/ 4-21-99	449645-06	-	-	U

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated